UNITED STATES DISTRICT COURT
DISTRICT OF MASSACHUSETTS

ASTELLAS INSTITUTE FOR REGENERATIVE MEDICINE, Plaintiff, v. IMSTEM BIOTECHNOLOGY, INC., XIAOFANG WANG, and REN-HE XU, Defendants.	C.A. No. 1:17-cv-12239

DEFENDANTS' TRIAL MEMORANDUM
WITH PROPOSED FINDINGS OF FACT AND CONCLUSIONS OF LAW

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I. INTRODUCTION

This lawsuit arises from a once-amicable scientific collaboration – between two of Plaintiff's scientists (Kimbrel and Lanza) and two Defendant scientists (Wang and Xu) – concerning protocols for making, and methods of using, human mesenchymal stem cells ("MSCs").

The gravamen of the case is about giving credit where credit is due, *i.e.* crediting *all* of the inventors of improvements over the prior art. Kimbrel and Lanza brought to the parties' scientific collaboration a basic, low-yield, four-step recipe for differentiating human embryonic stem cells into MSCs, a recipe that itself was built on others' work (some credited, some not). Drs. Wang and Xu's further changes to the protocol made the process work substantially better – improving yield, utility, safety, and therapeutic efficacy. Their effort, expertise, insight, and contributions warrant acknowledgment. The Patent Office has essentially agreed, expressly crediting one of their contributions and granting individual patent claims as to the others. Fortunately, beyond bruising egos, the parties' failure to name each other on their respective patents has not caused anyone any harm.

In sum, both sides' scientists made meaningful contributions to the art. The fact that they failed to fully acknowledge each other's contributions is a matter for the Court to correct, and Defendants respectfully request that it do so. Every inventor should be on every patent. Plaintiff's ancillary state law claims (which are little more than dressed up and preempted variations of the inventorship dispute) are without merit.

II. PROCEDURAL BACKGROUND

Plaintiff Astellas Institute for Regenerative Medicine ("Astellas") filed this action against Defendants ImStem Biotechnology, Inc. ("ImStem"), Dr. Xiaofang Wang ("Dr. Wang"), and Dr. Ren-He Xu ("Dr. Xu") (collectively, "Defendants"), originally alleging claims for correction of

inventorship of a patent under 35 U.S.C. § 256 (Count I – sole inventorship; Count II – joint inventorship), conversion (Count III), unjust enrichment (Count IV), unfair trade practices under Massachusetts General Laws Chapter 93A (Count V), misappropriation of trade secrets (Count VI), negligent misrepresentation (Count VII). (ECF 1).[1] Defendants filed counterclaims for correction of inventorship of two different patents under 35 U.S.C. § 256 and unjust enrichment. (ECF 91). Approximately two years into the case, Astellas sought leave to add a breach of contract claim (ECF 96), which the Court allowed over Defendants' objection. (*See* ECF 113 (Amended Complaint) at Count VII (breach of contract)).

The parties filed cross-motions for partial summary judgment (ECF 127, 131) and the Court *inter alia* granted partial summary judgment to Plaintiff as to Count II (joint inventorship), determining that Drs. Kimbrel and Lanza should be added to the '551 patent (on which Wang and Xu are already named inventors).

Shortly before the Final Pretrial Conference, Plaintiff announced they would no longer pursue their state law claims on misappropriation of trade secrets (Count VI), negligent misrepresentation (Count VII), and breach of contract (Count VIII), and has indicated that they will dismiss those claims with prejudice.

Accordingly, only Count I (correction of inventorship seeking sole inventorship), Count III (Conversion), Count IV (Unjust Enrichment), and Count V (Unfair Trade Practices under M.G.L. c. 93A) of Astellas' state law claims remain for adjudication.

[1] The original Complaint included co-plaintiff Stem Cell & Regenerative Medicine International, Inc. ("SCRMI"). SCRMI was a joint venture between Astellas' predecessor ACT (the relevant entity during the collaboration at issue in this case) and a South Korean company. ACT was eventually acquired by Astellas, which later also acquired co-Plaintiff SCRMI and any/all of its claims in this case.

III. PROPOSED FINDINGS OF FACT

A. The Parties

1. Plaintiff Astellas Institute for Regenerative Medicine is a U.S. affiliate of Astellas Pharma Inc ("Astellas"). Astellas is a global pharmaceutical company based in Tokyo, Japan, with its U.S. headquarters in Northbrook, Illinois. Plaintiff's principal place of business is 33 Locke Drive, Marlborough, MA 01752.

2. Defendant ImStem is a corporation organized and existing under the laws of Connecticut and its principal place of business at 400 Farmington Ave., R1808, Farmington, Connecticut 06030.

3. Defendant Dr. Ren-He Xu is a co-founder and former Chief Scientific Officer of ImStem. He is currently a Professor and Associate Dean at the University of Macau. Before moving to Macau (where he currently lives), Dr. Xu was an Associate Professor at the UConn Health Center, as well as Director of its Stem Cell Institute.

4. Defendant Dr. Xiaofang Wang is a co-founder and employee of ImStem and lives and works in Connecticut. Previously, he was a post-doc in Dr. Xu's lab and was a researcher at the University of Connecticut Health Center.

B. Basic Science

5. In nature, when an egg is fertilized by a sperm, the fertilized egg begins a process of division. The first cell splits into two cells, the two become four, the four become eight, and so on. At some point, these first "undifferentiated" (*i.e.* functionally identical) human embryonic stem cells ("hESCs") begin to differentiate; *i.e.* to express different genes and distinguish themselves into cell types that will eventually give rise to the full range of cells in the human body: bone, cartilage, nerves, skin, blood cells, organs, and tissues of all sorts. Scientists have for years studied the mechanisms of early cell differentiation. Much of it remains a mystery.

6. Mesenchymal stem cells ("MSCs") are quasi-differentiated cells that have the ability to become a wide range of bodily cells, such as bone, fat, and cartilage. While less pluripotent than precursor hESCs, they retain the ability to change and develop into a wide range of cell types.

7. MSCs occur in nature but they are transient. Scientists have reproduced them in the laboratory but the exact mechanisms and processes of natural MSC formation and differentiation was not fully understood in 2009. Indeed, as of 2009, scientists were still coming to terms with what exactly constituted a true, laboratory-made "MSC." Some scientists have since contested the value of the "MSC" moniker, given that the cell types are so variable.

8. At the time (and today) there were several known methods of obtaining or manufacturing MSCs or MSC-like cells. Each of the various MSC types were different and had different properties. At least during the 2010-2012 timeframe, the meaning of the term "MSC" was in flux and the field was rapidly developing.

9. Bone marrow derived MSCs ("BM-MSCs") are, as the name suggests, derived from bone marrow. This method involves isolating cells from bone marrow aspirate and performing density gradient centrifugation or adherence for isolation.

C. The Initial "Recipe"

10. In late 2009, three Astellas employees (Erin Kimbrel, Shi-Jiang Lu, and Robert Lanza) developed a protocol – essentially a recipe – for making a new kind of MSC-like cell. The protocol was built upon an earlier paper that Drs. Lu and Lanza had published in which they described starting with hESCs and differentiating them (using chemical stimulants) into embryoid bodies, then differentiating the embryoid bodies into cells called hemangioblasts. Now, in late 2009, Lu, Kimbrel, and Lanza conceived of adding a fourth step to the recipe:

further differentiating the hemangioblasts into MSCs, resulting in so-called "hemangioblast-derived MSCs" or "HB-MSCs."[2]

11. They did so *in vitro* (i.e., in the lab) and obtained cells that looked like MSCs. Critically, however: (i) Kimbrel and Lanza did not know whether the cells were true MSCs because they had no means of testing whether the cells would differentiate properly *in vivo* (i.e., using animal models), and (ii) they had not yet fully conceived of therapeutic uses of the cells. Kimbrel and Lanza were bench scientists, not clinicians. They lacked the skills and infrastructure to test their new cells *in vivo*. In early 2010, they froze the cells and put them in storage.

D. Wang and Xu's Prior Experience

12. Xu is a world-class stem cell scientist with notable recognition in the field of human embryonic stem cell. At the time of the collaboration with Astellas, Xu was an Associate Professor at the University of Connecticut Health Center. Prior to moving to Macau, Xu also served as Director of the Stem Cell Institute at the University of Connecticut Health Center. Xu is currently a professor of Health Sciences at the University of Macau. Xu has been listed as an author on many scientific articles regarding human stem cells.

13. Wang is a more junior scientist than Xu, but still maintains an impressive scientific resume. At the time of the collaboration with Astellas, Wang was working with Xu as a postdoctoral fellow at the University of Connecticut. Wang received his Ph.D. in Immunology from the University of Texas Health Science Center at Houston/ MD Anderson Cancer Center. For research experience, Wang has worked as a research assistant in the field of immunology at

[2] Many scientific teams were creating many protocols at this time, as means of exploring early stem cell differentiation. Notably, a team led by Dr. Slukvin at the University of Wisconsin had already differentiated HBs into MSCs by a different name. There was little remarkable about the Lu/Lanza/Kimbrel protocol.

the MD Anderson Cancer Center, and has done Postdoctoral research at the Yale University School of Medicine, also in the field of immunology.

14. Both Wang and Xu have training as medical doctors.

15. In late 2009 and early 2010 (well before they met Kimbrel and Lanza), Wang and Xu were in the process of writing a book chapter together on *inter alia* using hESC-derived MSCS to treat multiple sclerosis ("MS").

16. Xu and Wang had unique experience and facilities to administer the EAE animal model (*i.e.*, mice that had been genetically modified to mimic MS) at the time of the collaboration, which made them a desirable collaborator to the Plaintiff.

E. Wang and Xu's First Patentable Contribution: Treating Multiple Sclerosis

17. In the Spring of 2010, Lu encountered Wang and Xu at a conference and mentioned his team's new MSC-like cells.[3] In the course of those initial discussions, Wang suggested not only a way of testing the cells in mice *in vivo* but also suggested that the cells might be effective in treating MS, Wang's area of expertise. Wang and Xu were both M.D.s, attuned to real-world clinical treatments, not just the underlying biology, and had been on the lookout for such an opportunity for months; they had recently completed a book chapter on using MSCs to treat MS.

18. Over the next several weeks, Wang and Xu met with Kimbrel, obtained some samples of the purported "MSCs," designed a testing protocol for the EAE model, and began testing the cells.[4] Wang and Xu started sharing the ideas and results with Kimbrel and Lanza;

[3] Lu and Kimbrel worked at SCRMI, which was a joint venture between ACT and a South Korean company. Lanza was employed by ACT but oversaw Kimbrel's work at the SCRMI joint venture. ACT was later acquired by Ocata Pharmaceuticals and then Astellas, which later also acquired SCRMI.

[4] For expedience, Xu and Wang initially worked with another laboratory who performed the testing at their direction (that laboratory had the necessary permits). Once Xu and Wang got the necessary permits for conducting the tests

the parties were in regular contact. By late 2010, the experiments had started yielding favorable results.

F. Wang and Xu's Further Patentable Contributions: Improving the Recipe

19. As the experiments continued, the parties agreed that Wang should make the HB-MSCs himself, in-house, using the four-step hESC-EB-HB-MSC protocol that Kimbrel had given him. He quickly noticed that the yield using the "original" recipe was poor. The raw Lu/Lanza/Kimbrel protocol produced failed batches, poor-quality EBs, poor-quality HBs, and few final cells. Wang and Xu realized the protocol would never work at scale in any sort of clinical setting.

20. Wang and Xu therefore set about improving the recipe in order to advance the collaboration. They conceived, tested, and refined several improvements.

21. First, drawing upon their prior experience with serum-free and feeder-free cell cultures, Wang and Xu came up with the idea of adding a new chemical, 6-bromoindirubin-30-oxime (BIO) ("GSK3 inhibitor" or "GSK3i"), at a specific concentration to the initial culturing medium in which the hESCs were grown, essentially adding a new, precursor step to the protocol. GSK3i had never been used in this kind of four-step recipe and it created unexpectedly positive results in the later steps. By adding GSK3i to the cells before undertaking the first step, the revised protocol yielded better, more defined and tightly-ordered clusters of cells in the second (EB) step, and greater yield in the third (HB) and fourth (MSC) steps. Wang and Xu's use of GSK3i improved both quality and quantity, critical for use in a real-world clinical setting. Put simply, GSK3i had surprisingly beneficial downstream consequences.

with EAE model themselves, they did so. In any event, Wang and Xu developed the instructions and testing protocol for the EAE models.

22. Second, drawing upon their experience as MDs, Wang and Xu conceived of the idea of "mitotically inactivating" the HB-MSCs after they'd been formed – essentially adding a fifth step to the protocol. Wang and Xu's insight was that, contrary to what scientists believed at the time, the MSCs might have therapeutic use even if the MSCs were effectively sterilized and unable to subdivide (the ordinary behavior of MSCs) because they would nevertheless continue to secrete beneficial cytokines during their lifespan. Wang had conceived of the general idea before meeting Kimbrel and Lanza and decided that this recipe might be improved by it, by preventing the cells from causing tumors when injected into patients. (Years later, Astellas's own expert Dr. Brivanlou would call this "novel" and an "innovation – an invention.")

23. Third, after much thought and experimentation, Wang and Xu conceived of the idea of screening the cells created by the fourth step of the recipe (MSCs) based on measurements of the chemicals they secreted. In particular, Wang and Xu hypothesized that cells that secreted very low levels of IL-6 would be better for therapeutic use – contrary to some published reports that suggested IL-6 would be required – and that manufacturers should screen for and preferentially use such cells. This contribution likewise reflected Wang and Xu's expertise in MS and their background in real-world therapies, since low IL-6 expression would be beneficial for some conditions (*e.g.* MS) even if harmful for others.

24. IL-6 is a pleiotropic cytokine which produces either anti- or pro-inflammatory effects depending on the surrounding environment. IL-6 secreted by mesenchymal stem cells is associated with the induction of regulatory cells that promote immune tolerance, polarization of cells to a more anti- inflammatory phenotype, and/or enhanced expression of other anti-inflammatory molecules *in vitro*. Attenuation of inflammatory pathologies by administration of

ASCs is associated with elevated IL-6 and IL-10 levels in the affected tissue. In the case of MS, a very low IL-6 expression is likely to attenuate inflammatory pathologies.

25. Authentic MSCs are known to produce and express a myriad (100s to 1000s) of organic compounds ("paracrine factors") – of which IL-6 is a single factor – that each play a role in the manifestation of therapeutic outcomes. However, to specifically hone in on IL-6 as a factor that should not be expressed to enhance therapeutic outcomes in MS takes a high-level scientific expertise in MS and MS-treatment.

26. The idea of screening HB-MSCs for low IL-6 expression was not obvious in light of prior art in the 2010-12 timeframe. At the time, many scientists believed high IL-6 expression was beneficial to MSCs in a variety of ways, including proliferation, survival, differentiation, and migration. Low IL-6 might be harmful for some diseases, helpful to others. IL-6 can function in both a pro- and anti-inflammatory manner in different contexts. Singling out IL-6 as a marker from among the many proteins to screen for in the HB-MSCs – and "picking" the ones with low or no IL-6 – was not necessarily logical or obvious.

27. Numerous drafts of UConn grant application that Xu and Wang prepared (and which were reviewed by Astellas) in the December 2010 timeframe proposed that Xu and Wang would, among other things, study the production of IL-6 in the HB-MSCs that they were using for testing. Their idea was that MSCs with lower IL-6 would be better at treating MS, and therefore "selecting" MSCs with those characteristics was preferable for using with the EAE models.

28. Wang's laboratory notebook contains an entry dated June 1, 2012, which shows that he performed a "macroarray experiment" on different MSC samples, and he found that IL-6

expression is much lower in the HB-MSCs than in BM-MSCs. This prompted him to conduct more experiments to confirm his findings, including using flow cytometry.

29. Over the course of the next several months, Wang and Xu discussed these findings and began working on a paper regarding them.

30. At least by November 5, 2012, Wang told Kimbrel the results of his experiments regarding IL-6 and his plan to further test the importance of IL-6 in in-vitro and in-vivo experiment.

31. That same month, Kimbrel instructed Jian Chu, who was an Astellas employee, to test the HB-MSCs specifically for the presence or absence of IL-6. Chu did so, using a cytokine array. Kimbrel then presented the results from Chu's work regarding IL-6 to Astellas management.

32. In January, 2013 Kimbrel told Wang that she only has "a little bit of data" on IL-6 that "may compliment yours" but that she "hasn't followed up on it" and that "no one here is following up on IL6 either."

33. Fourth, Wang and Xu conceived of the idea of comparing the cells created in the fourth step to a reference MSC created using another, older recipe (so-called bone-marrow-derived MSCs or "BM-MSCs").

34. The idea of undertaking a comparison with BM-MSCs was not insubstantial. At the time, direct comparisons among cell types were rare. Everyone was in his or her camp. There was bone marrow-derived MSC camp, the adipose tissue-derived camp, the hESC-derived camp, etc. Making direct comparisons between cell populations at the time was rare. There wasn't a big body of literature. Subsequently, yes, but it was the exception at the time.

35. Moreover, the idea of comparing potency is tied up with Xu and Wang's idea of using the HB-MSCs cells for autoimmune and MS therapy. The potency comparison is donor dependent, age dependent, sex dependent, possibly race dependent, toxin smoking exposure, and media dependent. All of these things influence what the cells make. The notion of undertaking this particular potency assay was therefore an inventive contribution arising from the notion of using the cells to regulate the immune system to treat MS and potentially other autoimmune diseases.

36. Wang and Xu added a precursor step at the front end of the original Kimbrel/Lanza/Lu protocol and several steps at the back end – producing cells that were more numerous, more robust, and better adapted to transition from the laboratory to real-world clinical trials and use, making the process and the project more commercially viable. Wang and Xu's contributions were neither known in the art nor obvious in light of it. The regulation of stem cell development was extremely complicated and still largely unknown. Wang and Xu's improvements were unexpected, substantial, and meaningful, the product of insight, experience, and hard work.

37. By late 2011, Wang and Xu had substantially improved the protocol. They shared their data and certain of their improvements with Kimbrel and Lanza – not realizing that Kimbrel and Lanza were intending to poach the data and bake the improvements into a patent application without crediting Wang and Xu. Wang and Xu continued to run experiments, investigate the underlying science, investing hundreds of (unpaid) hours, and obtaining grants to fund the collaboration, all in the hope of publishing a scientific paper and advancing the field.

G. The Fraying of the Collaboration

38. Astellas began to undermine those plans. In 2011, ACT and Lanza took control of SCRMI and began trying to impose new, after-the-fact limitations on the collaboration,

including confidentiality obligations that were more aggressive than the parties had originally contemplated.

39. Relations deteriorated further in June 2012 when Lanza "accidentally" published some of the collaboration results at a conference in London without first obtaining permission from Xu and Wang, or even informing them what he was doing.

H. The Parties' Competing Patent Applications

40. The parties then began filing competing patent applications (prosecuted in parallel).

41. On November 30, 2011, Plaintiff filed U.S. Provisional Patent Application No. 61/565,358 ("'321 Provisional"). This '321 Provisional served as the basis for the patent applications that later become the '321 patent and the '956 patent.

42. The '321 Provisional included not only the original Kimbrel/Lanza/Lu protocol, but also (i) Wang and Xu's concept of using the resulting cells to treat MS; (ii) Wang and Xu's data showing treatment of the EAE model (i.e., MS-modelling mice); (iii) Wang and Xu's concept of mitotic inactivation – including a verbatim copy of Wang's original explanation previously drafted for a collaboration grant proposal; (iv) Wang and Xu's concept of IL-6 screening; and (v) Wang and Xu's concept of BM-MSC comparison. Kimbrel and Lanza did not name Wang and Xu as co-inventors, despite separately claiming many of the foregoing inventions. Nor did they name Lu. Nor did they name the scientist who had taught Kimbrel how to improve the fourth step by using a material called "matrigel," also separately claimed.

43. On or around January 20, 2012, which was well after the start of the collaboration, Dr. Lu, a colleague of Kimbrel and Lanza, sent a first draft of a material transfer agreement ("MTA") – which included confidentiality provisions about the parties work together – to Xu and Wang.

44. Subsequently, the parties negotiated about the terms of the MTA, which included the exchange of multiple redline copies of this agreement. The parties, however, never agreed to a final document, nor did they ever execute one.

45. On July 12, 2012, Xu and Wang filed U.S. Provisional Patent Application No. 61/670,787 ("'551 First Provisional Application").

46. This was a rough "provisional" application – drafted without the help of a lawyer – on certain aspects of their improved version of the original HB-MSC protocol.[5] They did not name Kimbrel and Lanza as co-inventors.[6]

47. On November 30, 2012, Plaintiff filed both U.S. Non-Provisional Patent Application No. 13/691,349 ("'321 Non-Provisional"), which would later mature into the '321 Patent, and Patent Cooperation Treaty Application No. PCT/US2012/067464 ("'321 PCT Application"). The '321 Provisional formed the basis for both the '321 Non-Provisional and the '321 PCT Application. Additionally, both the '321 Non-Provisional and the '321 PCT Application were substantially identical, including the description, drawings, scientific content, and the description of the four-step Lu/Kimbrel/Lanza protocol.

48. On February 11, 2013, Xu and Wang filed U.S. Provisional Patent Application No. 61/762,961 ("'551 Second Provisional Application"). This was also rough "provisional" application – drafted without the help of a lawyer – on aspects of their improved version of the original HB-MSC protocol.

49. In May 2013, Astellas learned that Wang and Xu had formed ImStem.

[5] In June 2012, Wang and Xu had formed defendant ImStem.

[6] The Court has since determined that Wang and Xu should have named Kimbrel and Lanza as co-inventors.

50. On May 21, 2013, Lu informed Lanza that he had learned (on May 12) that Defendants had formed their own stem cell company. Lu transmitted a link to ImStem's website to Lanza. In this email, Lu stated:

> Hi Bob,
>
> As we discussed last week in DC and today, I just learned (on May 12) that the UConn group we collaborated with our MSC project formed their own stem cell company. Here is the info for this company:
>
> Company Name: ImStem Biotechnology Inc
>
> Web Address: http://imstem.com

51. Astellas now knew that ImStem was directed to the development of hESC-derived MSCs to treat MS. Astellas even began monitoring the PTO for any filings or applications by Wang and Xu, and were concerned about ImStem.

52. On May 30, 2013, Plaintiff filed U.S. Non-Provisional Patent Application No. 13/905,526 ("'956 Non-Provisional"), which would later mature into the '956 Patent.[7] Claim 1 of the application included the invention of using HB-MSC cells to treat MS, the idea Wang had proposed in his first meeting in Marlborough, MA and the only concept for which Plaintiff had had data at the time of the original/underlying provisional application.

53. On June 6, 2013, the World Intellectual Property Organization ("WIPO") published the '321 PCT Application as International Application Publication No. WO2013/082543. In the published copy of the '321 PCT Application, Plaintiff claimed priority to the '321 Provisional Application.[8]

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[7] The '956 Non-Provisional was filed as a "Continuation-in-Part" of the '321 Non-Provisional, which means that the '321 Non-Provisional (and by extension the '321 Provisional) formed the basis for the '956 Non-Provisional but that the '956 Non-Provisional also described or depicted different subject matter that was absent from the '321 Non-Provisional.

[8] Strictly speaking, the '321 patent that issued claims priority to a parallel U.S. non-provisional filed at the same time.

54. The published copy of the '321 PCT Application publicly disclosed the contents of the four-step Lu/Kimbrel/Lanza protocol, the precise steps required to differentiate (1) hESCs into (2) embryoid bodies, then (3) hemangioblasts, then (4) MSCs. The '321 PCT contained a corresponding set of draft claims, also setting forth – publicly – this basic four-step Lu/Kimbrel/Lanza protocol.

55. Twenty-one days later, on June 27, 2013, Wang and Xu filed their own PCT application – Patent Cooperation Treaty Application No. PCT/US2013/048291 ("'551 PCT Application"). The '551 PCT Application was the basis for the '551 national stage ("non-provisional") and thus has the same specification and figures as the '551 patent.

56. The '551 PCT application was substantially revised from Xu and Wang's earlier filed provisionals. Wang had discovered the Kimbrel/Lanza application since filing the original provisionals, and substantially re-wrote the new '551 PCT application, this time with the assistance of counsel.

57. All of the Xu and Wang applications remained confidential (*i.e.* known only to the PTO, which in any event had already received the same information seven months earlier) until after the '321 patent application became public.

58. Wang and Xu did not disclose the protocol to their investors, none of whom would have understood it if they had. Wang and Xu instead sought and obtained investment based on their own, fundamentally different technology: T-MSCs (MSCs derived from trophoblasts, not hemangioblasts). An early draft of the ImStem business plan included cribbed language that referenced HB-MSCs, but that draft was never acted upon and quickly replaced. All later versions of the business plan focused on T-MSCs.

59. On June 28, 2013, Kimbrel sent her colleagues an email titled, "[K]eep eye on UConn patent pending," which stated:

> http//:www.ctmirror.org/story/stem-cell-grants-target-multiple-sclerosis-epilepsy-cancer. [S]ee story for bit on ImStem, the new company that our "collaborators" formed to continue exploring hESC-derived MSCs for Multiple Sclerosis.

I. The Paper Spat

60. Around this same time, a further dispute broke out between the parties concerning their shared work and collaboration. The parties had originally planned to jointly publish two papers: (1) a paper concerning the protocol and *in vitro* lab results; and (2) a paper concerning *in vivo* mouse model testing results. In August, 2013 Xu and Wang learned that Lanza and Kimbrel intended to publish a smaller paper early, without Xu and Wang as authors, which would contain a great deal of the information that was originally to be contained in an agreed upon larger paper, which would name Xu and Wang as authors. Having co-authorship with Xu and Wang on that paper was part of the "deal" for the collaboration and why Xu and Wang agreed to enter into it. In November 2013, in violation of their agreement with Xu and Wang, Kimbrel and Lanza unilaterally submitted the smaller paper to Stem Cells & Development. Xu and Wang were not listed as authors, nor were they given any credit.

61. Despite this, Xu and Wang continued to work with Lanza and Kimbrel towards the publication of a collaborative article regarding the results of their work together. The article was published in a less prestigious journal than the November 2013 article, and was largely preempted by that earlier article (which named Lanza and Kimbrel only as co-authors). After the July 2014 article, which names Lanza, Kimbrel, Xu and Wang as co-authors, but was published in the "lesser" journal, the parties stopped working together on HB-MSCs.

J. The Parties' Discovery of Each Other's Patent Applications

62. By at least February 4, 2014, Astellas discovered the aforementioned Xu/Wang patent application – PCT/US2013/04829 ("'551 PCT Application"), which had just published as WO2014/011407 – and immediately circulated it among senior management. Indeed, years later in their Amended Complaint, the Plaintiff would admit that they knew the content of Wang and Xu's patent application by February, 2014. [9]

63. Upon inspecting the '551 PCT Application, Plaintiff's senior management immediately determined that they had a potential legal claim against ImStem – as their lawyers would, years later, log the email attaching and discussing the '551 PCT Application as privileged because it "reflect[ed] legal advice *regarding anticipated litigation*." (emphasis added).

64. The discussions concerning litigation continued for months. In a lengthy June 2014 email exchange, Matthew Vincent, a former attorney then acting as Vice President of Business Development for Advanced Cell Technologies ("ACT") – the predecessor company to the Plaintiff– wrote to Plaintiff's senior management and at least one Board member:

> On a separate front, we have also looked at the recently published PCT applications (published Jan of this year), and think *we can make a case for why Erin should have been included as a co-inventor, and why ACT would be a co-owner of that patent.* If we were successful, it would make any partnering or sub-licensing by

[9] The '551 PCT Application was filed on June 27, 2013 and published as WO2014/011407 on January 16, 2014. That same '551 PCT application was then filed as a national stage ("non-provisional") application in the United States under 35 U.S.C. § 371 and assigned U.S. Patent Application No. 14/413,290 on January 7, 2015 (the '551 Non-Provisional Application), ultimately issuing as the '551 Patent. Simply put, the '551 PCT Application is substantively identical to the '551 Non-Provisional Application, and thus the '551 Patent. This is of necessity; an applicant for patent may not add new subject matter to a PCT, or national stage ("non-provisional") patent application after its filing date. Manual of Patent Examining Procedure ("MPEP") Appendix T, Patent Cooperation Treaty Articles 19(2), 28(2), 34(2)(b) ("The amendment shall not go beyond the disclosure in the international application as filed"), and 41(2) and Rules 66.2(a)(iv), 70.2(c), and 70.16(b)(i), 35 U.S.C. § 372(a) ("all questions of substance and . . . procedure in an international application designating the United States shall be determined as in the case of national applications regularly filed in the Patent and Trademark Office."), 37 C.F.R. § 1.53(b) ("No new matter may be introduced into an application after its filing date"), 37 C.F.R § 1.121(f) ("*No new matter*. No amendment may introduce new matter into the disclosure of an application."), 37 C.F.R § 1.125(a) ("a substitute specification . . . may be filed . . . if it is accompanied by a statement that the substitute specification includes no new matter."), 37 C.F.R § 1.821(g), and 37 C.F.R § 1.825(a).

> them impossible outside the US and tenuous in the US. (emphasis added)

That is, Plaintiff knew that Wang and Xu had formed ImStem. They knew that ImStem was operating in "their" field. They knew that Wang and Xu had filed a patent application on "their" protocol. They knew the contents of the '551 PCT Application (published as WO2014/011407 and then re-filed as a non-provisional and ultimately issuing as the '551 Patent). They knew that "Erin should have been included as a co-inventor." They nonetheless chose to delay:

> Bob (cc'd) had wanted to let this paper [to be co-published by Lanza, Kimbrel, Xu, and Wang] get to press before we considered that option any further.

Later that same night, Vincent emailed again. He provided detailed analysis of not only the harms Astellas had (allegedly) suffered but the legal claims and remedies available:

> The IP rights to protocol is now ours in the US, but only as a consequence to the restructured [sic]. I clarify this only because I want to make sure that we keep in the mind the distinctions of what we ACT can complain about – or even take legal action over – and what are the rights of SCRMI that would have to be enforced by SCRMI (in cooperation with CHA). *For example, any argument that protocol that we sent to UConn was intended by both parties to be kept confidential or was the property of SCRMI (despite no agreement) would be a right SCRMI would have to pursue.* Likewise, any rights we might want to argue should flow to us for inventions *based on the use* of the SCRMI MSCs at UConn (because the standard of practice would have been to use an MTA and that is UConn's policy) would be the right of SCRMI and not ACT. (emphasis added)

65. Thus, at least by June of 2014, Astellas was not only discussing its inventorship claims but also the ancillary torts that could colorably arise from the underlying alleged taking-of-technology conduct. Vincent spoke of a "confidentiality" claim "despite no agreement." He spoke of claims "based on the use" of the Plaintiff's intellectual property. Astellas was already

developing its legal strategy but it never notified Wang or Xu of their concerns or asked them not to use the technology.

66. Astellas continued to do nothing to protect its purported rights despite voicing concerns internally. On February 5, 2016, in response to an inquiry from a potential investor (Astellas), Lanza wrote to his in-house Senior Vice President of Business Development:

> They were so impressed with the results they tried to steal the technology [from us] and set up their own company. Matt [Vincent] can fill you in on the details, but we have an air-tight case against them. I believe *we were just waiting* until the appropriate time to serve them notice. (emphasis added)

67. Finally, more than four years after "keeping an eye" on their new competitor, three-and-a-half years after reviewing the '551 PCT Application and concluding it might cause "litigation," and more than three years after circulating in-house emails about their legal rights, Plaintiff filed suit.

68. The Complaint contained two counts for correction of inventorship, plus five state-law tort claims arising from the same work and collaboration. Plaintiff alleged that Defendants' filing of the '551 PCT Application gave rise to their state law claims.

69. Astellas filed an Amended Complaint on October 3, 2019, in which it (i) admitted it had known of the '551 PCT Application (i.e. the '551 Patent) since February 2104 and (ii) stated that knowledge of the information contained in the '551 Patent made them "aware of Defendants intended wrongful use of Plaintiff's confidential information."

K. The Prosecution History

70. As the parties' competing patent applications wended their way through their respective examinations at the PTO, the PTO spotted the overlap between their claims – and in the course of further examination addressed one of Wang and Xu's inventive contributions (GSK3i) and deemed it non-obvious.

71. Specifically, on June 13, 2016, the Defendants voluntarily disclosed the Lanza/Kimbrel patent application to the PTO as part of their own patent prosecution for what became the '551 patent. The Examiner – upon comparing the two applications – determined that the claims were substantively identical.[10] In a non-final Office Action mailed on July 28, 2016 the PTO therefore rejected the Defendants' claims as anticipated by Astellas' earlier-filed '321 application. In addition, the Examiner raised two obviousness rejections (including two respective secondary references).

72. In response to the PTO rejection, the Defendants filed a Response under 37 C.F.R. § 1.111 and amended claim 1 to affirmatively require the step of culturing hESCs in a serum-free medium "with at least one GSK3 inhibitor at a concentration ranging from 0.05 uM to 0.2 uM, wherein the hESCs are cultured in the absence of feeder cells."

73. The Defendants submitted arguments pointing out that the Astellas' application did not describe the GSK3 inhibitor limitations as amended, and that the amended claim (with GSK3i) was novel and non-obvious.

74. The Examiner agreed. In the Reasons for Allowance, the Examiner stated that the claims were allowable because "the claims now require the presence of a GSK3 inhibitor at a specific concentration that results in the production of hES-MSCs with the specific characteristics recited by the claims." The Examiner continued, "[t]his limitation overcomes the rejections of record [i.e., in the aforementioned 28 July 2016 non-final Office Action]." In short, according to the Examiner, the addition of GSK3i was sufficient to overcome the Examiner's

[10] At that point, the Defendants' claim 1 had recited the *optional* step of culturing hESCs with a GSK3 inhibitor. It was not yet a true limitation.

prior novelty and obviousness rejections. That is, the addition of GSK3i – one of Wang and Xu's contributions – was novel and non-obvious.[11]

75. Put differently, the PTO determined that the use of 0.05uM to 0.2 uM GSK3 inhibitor prior to undertaking the hESC-EB-HB-MSC differentiation protocol – the Defendants' contribution – was not only *an* inventive feature, it was the *only* inventive feature of the claim. Lanza and Kimbrel contributed nothing to that inventive feature.

L. ImStem's Rival "T-MSC" Technology

76. While all of the foregoing was taking place – the collaboration on HB-MSCs, competing patents regarding the basic and improved versions of the HB-MSC recipe, the formation of ImStem, etc. – Wang and Xu were busily working on a different project altogether.

77. In 2002, Xu was one of the first scientists to differentiate human embryonic stem cells (hESCs) into trophoblasts using a molecule called BMP4, a discovery that was later published in Nature Biotechnology. Trophoblasts are the earliest differentiated cell type formed during embryogenesis and are progenitor cells for the placenta.

78. Some time after Wang joined Xu's lab in 2008, Xu proposed that they explore using trophoblasts to derive MSCs (to create what they termed "T-MSCs").

79. Dr. Xu's prior (2002) paper about differentiation into trophoblasts was the "jumping off point" for this work, much like (according to Astellas) the 2007 Lu/Lanza Nature Methods paper about differentiation into hemangioblasts was for Astellas' HB-MSC protocol that was developed in 2010. Although Drs. Xu and Wang continued their T-MSC work during the time they were collaborating with Astellas on HB-MSCs, their T-MSC work was separate.

[11] Wang and Xu also filed a declaration under 37 C.F.R. § 1.131 "swearing behind" the Lanza and Kimbrel application, but the declaration was mooted by the Examiner's determination that the use of GSK3i was novel and non-obvious. It is not evident from the record that the Examiner even considered or reviewed the declaration for any particular purpose.

80. The ImStem method of deriving T-MSCs is a different method from the one used to derive HB-MSCs using hemangioblasts as an intermediate. Trophoblasts are the progenitor cells for the placenta. Using the T-MSC method means a single cell clone can lead to an endless supply of T-MSCs that may benefit a large patient population with various autoimmune diseases while maintaining high immunosuppressive potency, consistent quality, low immunogenicity and low cost.

81. ImStem's T-MSC protocol requires 6-11 days to derive cells, which is faster than other methods that may need 20-30 days. Additionally, when compared to MSCs derived from adult tissues, T-MSCs better maintain potency after culture, demonstrate higher efficacy and migration abilities, and trigger less immunogenic response which lends to broader application. ImStem's T-MSC technology acts as a versatile platform that can be applied to whole cell therapeutics, localized tissue repair, drug delivery systems, and other techniques.

82. By the spring of 2012, Xu and Wang's T-MSC method had been developed and was the basis for forming ImStem in 2012.

83. Several ImStem business plans (including one from July 2012) and investor presentations highlight the advantages of hES-MSCs to adult tissue-derived MSCs, as well as technological advantages of the ImStem trophoblast differentiation method over other types of MSCs.

84. In 2013, the Connecticut-based Regenerative Medicine Research Fund Grants Program awarded ImStem a $1.13 million grant for its plan to continue its research into T-MSCs. The proposal that ImStem submitted highlighted its goal of applying the T-MSC method to test hES-MSCs in a pre-clinical setting; there is no reference in the document to HB-MSCs

85. In 2014, Dr. Wang attended a New York Young Start-up Venture Summit, where he highlighted various features of the T-MSC technology, including: T-MSCs' ability to produce unlimited MSCs from a single ES cell; T-MSC efficacy and outperformance of other adult-MSC methods; the variety of diseases and applications the T-MSC platform targets; and ImStem's cGMP manufacturing with an easier U.S. Food & Drug Administration ("FDA") path. The document's only reference to HB-MSC technology appears in a comparison of cell yield among different MSC derivation methods, which shows that T-MSCs have a higher cell yield.

86. In 2014, ImStem entered pre-pre-IND discussions for its T-MSC treatment for MS with the FDA.

87. ImStem used an embryonic stem cell line that it licensed and obtained from a third party (not Astellas) to derive T-MSCs.

88. Xu and Wang sought patent protection for their T-MSC technology. That patenting effort was (and continues to be) substantial:

- On July 12, 2012, Xu and Wang filed provisional application 61/670,192 with the PTO. It describes and claims a method for deriving MSC from hESCs through a trophoblast intermediate. ImStem currently owns this application.

- On August 17, 2012, Xu and Wang filed provisional application 61/684,509 with the PTO. It also describes and claims a method for deriving MSCs from hESCs through a trophoblast intermediate. ImStem currently owns this application.

- On July 11, 2013, Xu and Wang filed International Application No. PCT/US13/050077 with the USPTO Receiving Office, which claims priority to 61/670,192 and 61/684,509, and which was published by the World Intellectual Property Organization ("WIPO") on January 16, 2014 as WO2014/011881. The application generally relates to T-MSCs. ImStem currently owns this application.

- On January 7, 2015, Xu and Wang filed U.S. Application No. 14/413,297 as a national stage entry of the PCT/US13/050077 application, which also claims priority to provisional applications 61/670,192 and 61/684,509. ImStem currently owns this application. The 14/413,297 application published on July 9, 2015 as US2015/0191699 and ultimately issued as U.S. Patent No. 9,725,698, titled "Trophoblast-Derived Mesenchymal Stem Cells (T-MSCS) Produced from Human

Embryonic Stem Cells, Methods and Uses Thereof." That patent lists Xu and Wang as inventors and is currently owned by and assigned to ImStem.

- On June 27, 2017, Xu and Wang filed U.S. Application No. 15/635,022 with the PTO as a continuation of the 14/413,297 application, which also claims priority to provisional applications 61/670,192 and 61/684,509. ImStem currently owns this application. The 15/635,022 application published on October 12, 2017 as US2017/0290864 and ultimately issued as U.S. Patent No. 10,226,488, titled "Mesenchymal-Like Stem Cells Derived from Embryonic Stem Cells, Methods and Uses Thereof." That patent lists Xu and Wang as inventors and is currently owned by and assigned to ImStem.

- On January 23, 2019, Xu and Wang filed application 16/254,986 with the PTO as a continuation of the 15/635,022 application, which also claims priority to provisional applications 61/670,192 and 61/684,509. The application generally relates to T-MSCs. ImStem currently owns this application. The 16/254,986 application published on June 6, 2019 as US2019/0167733.

M. Astellas Delays Filing Suit

89. More than four years after "keeping an eye" on their new competitor, three-and-a-half years after reviewing the '551 PCT Application and concluding it might cause "litigation," and more than three years after internally articulating their legal rights, Astellas finally filed suit.

N. Astellas Suffered No Harm

90. Astellas' failure to timely act reflected the fact that it was suffering (and has suffered) no harm. Aside from causing a few bruised egos, Wang and Xu's failure to name Kimbrel and Lanza has cost Astellas nothing. The original provisional application was disclosed only to the PTO.

91. The revised '551 PCT Application became public only after Kimbrel and Lanza had already filed and made public their own application – which publicly disclosed Plaintiff's initial recipe. Wang and Xu's provisional patent applications were likewise not accessible to the public until July 23, 2015, the date of publication of the corresponding U.S. National Stage Application of PCT/US2013/048291 (i.e., U.S. Patent Application 14/413,290).

92. Put simply, the raw Lu/Kimbrel/Lanza protocol – allegedly taken by Defendants and baked into the '551 patent – was public prior art by the time Wang and Xu filed their '551 PCT application.

93. Since then, neither the Defendants nor the Plaintiff have ever licensed or commercialized any process or product that employs any of the patents-in-suit. Indeed, the only damages to which Astellas points are the investments made in ImStem, but those had everything to do with Wang and Xu's other, competing "T-MSC" technology, not the HB-MSC technology – and certainly not the low-yield, unimproved version that Kimbrel and Lanza (and Lu) actually created.

94. Astellas' damages expert, Dr. Bell, does not offer any opinion that Astellas has suffered any actual losses, compensatory damages, incidental damages, or that Astellas has suffered any lost profits. In fact, Astellas has not commercialized or obtained any revenue from the inventions claimed in the '321 or '956 patents or, in fact, HB-MSCs. Nor has ImStem commercialized or obtained any revenue from inventions claimed in the '551 patent or HB-MSCs in general.

95. Astellas' claimed damages are based on calculations of the "implied value" of ImStem at various points in time, not on the actual money that ImStem took in from investors. The lynchpin of Astellas' damages theory is that 100% of the value of ImStem must be attributed to Defendants' allegedly improper actions. This is incorrect.

96. First, Astellas' assumption that 100% of ImStem's "implied value" is inconsistent with the facts, which demonstrate that ImStem has long been developing and pursuing T-MSCs, which represent a large source of independent value. In fact, ImStem's lead investor decided to invest because of Dr. Xu's stellar reputation and the company's work with T-MSCs, not HB-

MSCs.[12] In fact, the "entire" value of ImStem reflects years of independent development efforts and their own contributions. These examples demonstrate that, at minimum, there needed to have been some apportionment done of ImStem's "implied value" – which Astellas never did.

97. Indeed, ImStem's rival T-MSC technology may explain Astellas' desire to file suit – *i.e.* to use litigation to knock out a competitor. While Astellas' own work on MS treatments has slowed, ImStem's has advanced. In March, 2020, the FDA cleared ImStem's IND for its T-MSC treatment for the treatment of MS.

98. Second, Astellas is wrong to focus on the "implied value" of ImStem – which is just adding up all of the shares of the company (those that investors have purchased and those which the company holds) to arrive at a large number. ImStem has never turned a profit. Giving Astellas damages for money that ImStem has not actually collected from investors or obtained as revenue, but rather which exist only on paper, is unfair and inappropriate.

99. To the extent that Defendants were liable for any of the state law claims (they are not), and Astellas has suffered any damages (it has not), the proper damages framework is the one that ImStem has proffered – a hypothetical negotiation between the parties in the summer of 2010 (which is the beginning of the collaboration) for a lump small sum license to Astellas' purported intellectual property.

[12] Another source of value is Wang and Xu's modifications to Astellas' base HB-MSC protocol, as reflected in the '551 patent.

IV. PROPOSED CONCLUSIONS OF LAW

A. Plaintiff's Inventorship Claim ('551 patent) and Defendants' Inventorship Counterclaims ('321 and '956 patent)

1. Law

100. "A person who alleges that [he or she] is a co-inventor of the invention claimed in an issued patent who was not listed as an inventor on the patent may bring a cause of action to correct inventorship in a district court under 35 U.S.C. § 256." *Vapor Point LLC v. Moorhead*, 832 F.3d 1343, 1348 (Fed. Cir. 2016) (quoting *Eli Lilly & Co. v. Aradigm Corp.*, 376 F.3d 1352, 1357 n.1 (Fed. Cir. 2004)), *cert. denied sub nom. Nanovapor Fuels Grp., Inc. v. Vapor Point, LLC*, 137 S. Ct. 1121 (2017); *see* 35 U.S.C. § 256 (2012) (permitting correction of inventorship "[w]henever . . . through error an inventor is not named in an issued patent"). "Inventorship is a mixed question of law and fact: The overall inventorship determination is a question of law, but it is premised on underlying questions of fact." *Eli Lilly*, 376 F.3d at 1362. Since "[p]atent issuance creates a presumption that the named inventors are the true and only inventors," to establish co-inventorship, the alleged co-inventor "must prove [his or her] contribution to the conception of the claims by clear and convincing evidence." *Ethicon, Inc. v. U.S. Surgical Corp.*, 135 F.3d 1456, 1460–61 (Fed. Cir. 1998).

101. Joint inventorship "is one of the muddiest concepts in the muddy metaphysics of the patent law." *Mueller Brass Co. v. Reading Industries, Inc.*, 352 F.Supp. 1357, 1372 (E.D. Pa. 1972). "Inventorship is a mixed question of law and fact: The overall inventorship determination is a question of law, but it is premised on underlying questions of fact." *Eli Lilly & Co. v. Aradigm Corp.*, 376 F.3d 1352, 1362 (Fed. Cir. 2004). "[T]he critical question for joint conception is who conceived, as that term is used in the patent law, the subject matter of the claims at issue." *Falana v. Kent State University*, 669 F.3d 1349, 1357 (Fed. Cir. 2012) (*citing*

Ethicon, Inc. v. U.S. Surgical Corp., 135 F.3d 1456, 1460 (Fed. Cir. 1998)). "A contribution to one claim is enough" to qualify a joint inventor. *Id.* "All inventors, even those who contribute to only one claim or one aspect of one claim of a patent, must be listed on that patent." *Vapor Point LLC v. Moorhead*, 832 F.3d 1343, 1348–49 (Fed. Cir. 2016), *cert. denied sub nom. Nanovapor Fuels Grp., Inc. v. Vapor Point*, LLC, 137 S. Ct. 1121 (2017); *see Fina Oil and Chemical Co. v. Ewen*, 123 F.3d 1466, 1473 (Fed. Cir. 1997) ("One need not alone conceive of the entire invention, for this would obviate the concept of joint inventorship.").

102. The Federal Circuit has explained that "[a]ll that is required of a joint inventor is that he or she (1) contribute in some significant manner to the conception or reduction to practice of the invention, (2) make a contribution to the claimed invention that is not insignificant in quality, when that contribution is measured against the dimension of the full invention, and (3) do more than merely explain to the real inventors well-known concepts and/or the current state of the art." *Israel Bio-Eng'g Project v. Amgen, Inc.*, 475 F.3d 1256, 1263-64 (Fed. Cir. 2007) (quoting *Pannu v. Iolab Corp.*, 155 F.3d 1344, 1351 (Fed. Cir. 1998)). A co-inventor does not need to make a contribution to every claim of a patent. *Ethicon*, 135 F.3d at 1460. Nor does a co-inventor need to contribute to the conception of all the limitations in a single claim. *Eli Lilly*, 376 F.3d. at 1361. "The determination of whether a person is a joint inventor is fact specific, and no bright line standard will suffice in every case." *Fina Oil & Chem.*, 123 F.3d at 1473.

2. Xu and Wang Contributed Significantly to the '551 Patent and Should Remain Named Inventors

103. As noted above, Xu and Wang started with a basic four-step protocol that produced poor results and low yield and substantially improved it. One of those improvements (use of 0.05uM to 0.2 uM GSK3 inhibitor prior to undertaking the hESC-EB-HB-MSC differentiation protocol) had never been deployed in this kind of four-step recipe and it created

unexpectedly positive results in the later steps. It was never part of the Lu/Lanza/Kimbrel protocol. By adding GSK3i to the cells before undertaking the first step, the revised protocol yielded better, more defined and tightly-ordered clusters of cells in the second (EB) step, and greater yield in the third (HB) and fourth (MSC) steps. Wang and Xu's use of GSK3i improved both quality and quantity, critical for use in a real-world clinical setting. Put simply, GSK3i had surprisingly beneficial downstream consequences.

104. This contribution is sufficient to warrant Wang and Xu's (continued) presence on the '551 patent.

105. Further, the Examiner's finding that the addition of GSK3i was non-obvious during the prosecution of the '551 patent (in the "Reasons for Allowance") is itself powerful evidence that Wang and Xu's contributions was non-obvious and not insubstantial.

106. Before a claim in a U.S. non-provisional patent application can issue as a patent it must undergo rigorous examination by a patent examiner at the PTO. Examination includes an evaluation of whether the claims satisfy the statutory requirements for patenting, including 35 U.S.C. § 102 (novelty), and 35 U.S.C. § 103 (nonobviousness). Novelty and obviousness are considered with respect to information that is known, and that predates the invention (*i.e.*, "prior art").

107. In order for an Examiner to conclude that an obviousness issue exists under 35 U.S.C. § 103, the Examiner must conclude that the differences between the claimed invention and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the pertinent art. *See* MPEP § 2141(I); *Graham v. John Deere Co.*, 383 U.S. 1 (1966). A conclusion of obviousness requires consideration of the scope and content of the prior art, the differences between the prior art and

the claimed invention, the level of ordinary skill in the field of the invention, and any relevant objective considerations. *See* MPEP § 2141(II); *KSR International Co. v. Teleflex Inc.*, 550 U.S. 398, 406 (2007) (citing *Graham v. John Deere Co.*, 383 U.S. 1, 17–18 (1966)).

108. In the event a Patent Examiner raises a prior art rejection on the basis of novelty (i.e., anticipation) or obviousness, the applicant is entitled to present arguments rebutting the examiner's conclusions and/or submit amendments to the claims in order to obviate the rejection. *See* MPEP §§ 706-707. For example, an applicant can amend the claims to include an element not described or suggested by the cited art. *See* MPEP § 714. Once presented with such an amendment, the Examiner will again consider the claims in view of the statutory requirements. If the Examiner concludes that the amendment adds enough so that the amended claims are both novel and non-obvious over the prior art, the Examiner will then allow the claims with an explanation of the Reasons for Allowance as required by 37 C.F.R. § 1.104(e). *See* MPEP § 1300.

109. The foregoing process happened here. Plaintiff filed the '321 Provisional Application prior to the Defendants' '551 First Provisional Application. Neither the '321 Provisional Application nor any of its descendants describe or suggest the step of "culturing human embryonic stem cells (hESC) in a serum free medium comprising at least one GSK3 inhibitor at a concentration ranging from 0.05 uM to 0.2 uM…," which is recited in the '551 patent.

110. The Examiner compared Plaintiff's '321 PCT Application (published as WO2013/0825543) to Defendants' then-pending application (and other prior art of record) and found that that Defendants' additional requirement of using a GSK3 inhibitor at a specific concentration was sufficiently novel and non-obvious to entitle Wang and Xu to a patent (which

became the '551 patent). As noted above, the Examiner stated that the addition of GSK3i was sufficient to overcome the Examiner's prior novelty and obviousness rejections. That is, the addition of GSK3i – one of Wang and Xu's contributions – was novel and non-obvious.

111. PTO determined that the use of 0.05uM to 0.2 uM GSK3 inhibitor prior to undertaking the hESC-EB-HB-MSC differentiation protocol – the Defendants' contribution – was not only *an* inventive feature, it was the *only* inventive feature of the claim. Lanza and Kimbrel contributed nothing to that inventive feature.

112. Given that Wang and Xu's contribution was non-obvious and sufficiently substantial to warrant an entire patent in the eyes of the PTO, the Court finds that Wang and Xu's contribution was more than sufficient to warrant their (continued) inclusion as named inventors.

3. Xu and Wang Contributed Significantly to the '321 Patent and Should Be Named Inventors

113. As noted above, Xu and Wang started with a basic four-step protocol that produced poor results and low yield and substantially improved it.

114. Several of their improvements appear in the claims of the '321 patent. Claim 17 claims "The mesenchymal stromal cells of claim 14, wherein the mesenchymal stromal cells are mitotically inactivated." As noted above, Wang and Xu contributed this idea. Wang and Xu's insight was that the MSCs might have therapeutic use even if the MSCs were effectively sterilized and unable to subdivide (the ordinary behavior of MSCs) because they would nevertheless continue to secrete beneficial cytokines during their lifespan. Plaintiff's own expert, Dr. Brivanlou, has candidly admitted that this was "innovation – an invention."

115. Claim 18 reinforces the significance of the contribution: "The mesenchymal stromal cells of claim 17, comprising at least 10^6 mesenchymal stromal cells and a

pharmaceutically acceptable carrier." The claim is directed to therapeutic use, pharmaceutical treatment – Drs. Xu and Wang's area of comparative expertise, both of whom were skilled in making laboratory phenomena function at real-world scale.

116. Claim 21 recites: "The composition of claim 14, wherein the mesenchymal stromal cells have a potency in an immune regulatory assay that is greater than the potency of bone marrow derived mesenchymal stromal cells." This reflects Drs. Xu and Wang's idea of comparing the new cells to BM-MSCs.

117. These improvements did more than recite well-known phenomena in the art. This was a complex and poorly understood scientific field. Papers and prior art pointed in multiple directions. With transplantation and regenerative medicine, transplanted cells were generally not mitotically inactivated. Drs. Wang and Xu's idea was different, relying on their understanding of the natural short lifespan of the MSC cells and their guess (correctly as it turns out) that the HB-MSC secretions would provide the therapeutic benefit. Nor was this contribution obvious. At the time, mitotic inactivation was not widely used and had not been used in connection with stem cells. ESC-derived MSCs were not as widely understood or used as adult-cell-derived MSCs, in which the presence of stray precursor cells would not create a substantial risk of tumorigenesis. It was not a common routine practice.

118. Further, certain factors produced by the cells quiet inflammation, primarily by altering immune cell production and activity. The science underlying these processes was not well understood. It would have been reasonable to fear that mitotic inactivation could alter the secretome, the collection of secretions – proteins, growth factors, RNA, DNA. In some cases, using mitotically inactivated cells *in vivo* could have unwanted effects on cell function and

behavior, such as decreased cell survival, decreased engraftment, changed or decreased secretions, changed or decreased cell trafficking.

119. The Court finds that Wang and Xu's contributions to the claims of the '321 patent were meaningful, non-obvious, not insubstantial and sufficient to warrant their inclusion a named inventor.

4. Xu and Wang Contributed Significantly to the '956 Patent and Wang Should Be Named as an Inventor

120. As noted above, Wang (and Xu) contributed the idea of using Lanza and Kimbrel's not-yet-tested cells to treat multiple sclerosis at the very outset of the collaboration. Defendants have met their burden to establish that Wang should be added as a named inventor on the '956 patent.[13]

121. This contribution appears in several claims of the issued '956 patent. Claim 3 of the '956 patent claims using the cells generated in claim 1 to treat diseases or disorders "wherein the disease or disorder is selected from multiple sclerosis . . ." Claim 1 goes on to list 70 other diseases, an incredible and far-flung range of unrelated conditions ranging from fractured tibias to Crohn's disease to Lupus.

122. Claim 4 likewise recites: "The method of claim 1, wherein the disease or disorder is uveitis, an autoimmune disorder, an immune reaction against allogeneic cells, multiple sclerosis, bone loss, cartilage damage, or lupus."

123. Notably, the only condition for which the applicants (Lanza and Kimbrel) had actual data at the time of the original '956 Provisional Application was Xu and Wang's data from mice that had been genetically altered to mimic MS. Lanza and Kimbrel were not yet in

[13] In the Court's ruling on Defendants' motion to amend their counterclaims (ECF 85), it ruled that, for procedural reasons, Defendants could not seek to add Xu to the '956 patent. *See* ECF 85 at 10-11.

possession of any other invention, merely speculation that the cells might work on the longer list (again: a list developed at the time of filing, *i.e.* years after Xu and Wang had suggested the parties try treating MS). MS was the seminal idea, the original idea that took these cells from a laboratory curiosity with vague dreams attached to a concrete idea and a real invention.

124. The idea of using the HB-MSCs therapeutically to treat autoimmune diseases, including MS, was a meaningful, non-obvious, and not insubstantial contribution to the '956 patent.

125. Further, Xu and Wang's process improvements – developed once the collaboration was up and running – also appear in the claims.

126. Claim 5 of the '956 patent claims the method of claim 1," wherein the mesenchymal stromal cells (a) are mitotically inactivated; . . ."

127. As noted above, this was Xu and Wang's idea. And as noted above, it was significant and non-obvious.

128. Claim 9 of the '956 patent claims the method of claim 1, "wherein the mesenchymal stromal cells . . . (f) in a resting state, express mRNA encoding interleukin-6 at a level which is less than ten percent of the IL-6 mRNA level expressed by mesenchymal stromal (IL-6) cells, in a resting state, derived from bone marrow or adipose tissue;"

129. As noted above, this was Xu and Wang's idea. After much thought and experimentation, Wang and Xu conceived of the idea of screening the cells created by the fourth step of the recipe (MSCs) based on measurements of the chemicals they secreted. In particular, Wang and Xu hypothesized that cells that secreted very low levels of IL-6 would be better for therapeutic use, and that manufacturers should screen for and preferentially use such cells. This contribution likewise reflected Wang and Xu's expertise in MS and their background in real-

world therapies, since low IL-6 expression would be beneficial for some conditions (*e.g.* MS) even if harmful for others.

130. The idea of screening for a marker of low IL-6 expression is a substantial contribution to the '956 patent. Authentic MSCs are known to produce and express a myriad (100s to 1000s) of organic compounds ("paracrine factors") – of which IL-6 is a single factor – that each play a role in the manifestation of therapeutic outcomes. However, to specifically hone in on IL-6 as a factor that should not be expressed to enhance therapeutic outcomes in MS takes a high-level scientific expertise in MS and MS-treatment.

131. The idea of screening HB-MSCs for low IL-6 expression was not obvious in light of prior art in the 2010-12 timeframe. At the time, many scientists believed high IL-6 expression was beneficial to MSCs in a variety of ways, including proliferation, survival, differentiation, and migration. Low IL-6 might be harmful for some diseases, helpful to others.

132. Likewise, for the EAE model, there was no preconceived consensus in the 2010-12 timeframe as to how IL-6 would work. It was unclear which cytokine contributes to immune response. Wang and Xu's background in autoimmunity allowed them to understand that data and conclude that IL-6 is a driver for the immune response.

133. Finally, Claim 10 of the '956 patent claims the method of claim 1, "wherein the mesenchymal stromal cells have a potency in an immune regulatory assay greater than the potency of bone marrow derived mesenchymal stromal cells."

134. As noted above, this was Xu and Wang's idea. Further, while smaller than the other contributions, the idea of undertaking a comparison with BM-MSCs was not insubstantial. At the time, direct comparisons among cell types were rare. Everyone was in his or her camp. There was bone marrow-derived MSC camp, the adipose tissue-derived camp, the hESC-derived

camp, etc. Making direct comparisons between cell populations at the time was rare. There was not a big body of literature. Subsequently, yes, but it was the exception at the time.

135. Moreover, the idea of comparing potency is tied up with Xu and Wang's idea of using the HB-MSCs cells for autoimmune and MS therapy. The potency comparison is donor dependent, age dependent, sex dependent, possibly race dependent, toxin smoking exposure, and media dependent. All of these things influence what the cells make. The notion of undertaking this particular potency assay was therefore an inventive contribution arising from the notion of using the cells to regulate the immune system to treat MS and potentially other autoimmune diseases.

136. The Court finds that Wang and Xu's contributions to the claims of the '956 patent were meaningful, non-obvious, not insubstantial and sufficient to warrant Wang's inclusion as a named inventor.

B. Astellas' State Law Claims

1. Conversion (Count III)

137. As a preliminary matter, Astellas' claim for conversion (Count IV) is time-barred. "[A]ctions of tort . . . shall be commenced only within three years next after the cause of action accrues." G.L. c. 260, § 2A.[14] *See Patsos v. First Albany Corp.*, 433 Mass. 323, 327–328 n. 6, 741 N.E.2d 841 (conversion actions are based in tort, to which a three year statute of limitations applies); *see also Solomon v. Birger*, 19 Mass. App. Ct. 634, 638, 477 N.E.2d 137, 141 (1985) (actions based on deceit, including misrepresentation, are based in tort, and a three year statute of limitations applies).

138. The accused taking-of-technology took place the moment Xu and Wang filed and claimed as their own the provisional patent application that would eventually mature into the '551 patent. *Nortek, Inc. v. Liberty Mut. Ins. Co.*, 65 Mass. App. Ct. 764, 770–71, 843 N.E.2d 706, 712 (2006) (tort action accrues the date the plaintiff suffers injury). That allegedly wrongful activity took place on July 12, 2012. The Plaintiff say as much; they contend that Wang and Xu claimed Plaintiff's (alleged) technology as their own by seeking patent protection for a method for producing human embryonic stem cell-derived mesenchymal stem cells from a hemangioblast intermediary in the '551 PCT Application.

139. For conversion, the tort accrues the moment another asserts an intentional act of dominion inconsistent with the rights of the owner. *See In re Hilson*, 448 Mass. 603, 611, 863 N.E.2d 483 (2007) ("[t]he elements of conversion may be established by a showing that one person exercised dominion over the personal property of another, without right, and thereby deprived the rightful owner of its use and enjoyment"); *Blake v. Prof'l Coin Grading Serv.*, 898

[14] There is no dispute that Massachusetts law applies.

F. Supp. 2d 365, 386 (D. Mass. 2012); *see also Spooner v. Manchester*, 133 Mass. 270, 273–74 (1882) (finding conversion occurred the moment "there was an intentional act of dominion exercised . . . inconsistent with the right of the owner.") Here, under the Plaintiff's theory, that act of dominion occurred the moment Wang and Xu filed their PCT application and told the world that the inventions in their PCT application (*i.e.* the eventual specification of the '551 patent) belonged to them. Under the claims advanced by the Plaintiff, Wang and Xu had commandeered Astellas' ideas and content, claimed them as their own, and sought to use them for patenting purposes. Wang and Xu had not only (allegedly) converted Astellas' intellectual property the moment they filed their application, they converted the resulting patent application. Patent applications are property. *Figueroa v. United States*, 57 Fed. Cl. 488, 502 (2003), *aff'd*, 466 F.3d 1023 (Fed. Cir. 2006); *Winchester v. Comm'r*, 27 B.T.A. 798, 801 (1933) ("[i]t is now well settled that patent applications are property.").[15]

140. Conversion thus applies to patent applications, not just issued patents. *See, e.g.*, *Palmer v. Neal*, 602 F. Supp. 882, 885 (N.D. Ga. 1984) (conversion claim applicable to application, before issuance); *WesternGeco v. Ion Geophysical Corp.*, No. CIV.A. 09-CV-1827, 2009 WL 3497123, at *5 (S.D. Tex. Oct. 28, 2009) (same); *Auburn Univ. v. Int'l Bus. Machines, Corp.*, 716 F. Supp. 2d 1114, 1117 (M.D. Ala. 2010) (same); *Ferring B.V. v. Allergan, Inc.*, 932 F. Supp. 2d 493, 510 (S.D.N.Y. 2013) (conversion likely occurred even before application). If the Court were to accept Plaintiff's claim that Wang and Xu commandeered Astellas' ideas and content, claimed them as their own, and sought to use them for patenting purposes, then Wang

[15] They can be licensed, bought, sold, and mortgaged like other property. 35 U.S.C. § 261. The can make up the *res* of trust. *Conway v. White*, 292 F. 837, 843 (2d Cir. 1923); Restatement (Second) of Trusts § 82. They can even be assigned in bankruptcy. *Keen, Inc. v. Gecker*, 264 F. Supp. 2d 659, 662-63 (N.D. Ill. 2003).

and Xu "converted" Astellas' intellectual property the moment they filed their first application with the United States PTO for the technology at issue.

141. As such, the Plaintiff's cause of action in conversion accrued on July 12, 2012. Three years from the date of accrual would have been July 12, 2015. The Plaintiff did not file the instant action until November 13, 2017, over 5 years after the cause of action had accrued.

142. Nor can the Plaintiff claim the statute of limitations was tolled by lack of knowledge. *Cf. Riley v. Presnell*, 49 Mass. 239, 244 (1999) (statute of limitation may be tolled only until the time the plaintiff knows or should know of the injury). As noted above, Astellas knew that Wang and Xu had formed ImStem and knew of ImStem's corporate goals by May 2013, *i.e.* more than four years before filing suit.

143. Under the Massachusetts discovery rule, a plaintiff need not know every offending fact constituting his or her claim. *Riley*, 409 Mass. at 243. Nor does the plaintiff need to be aware of his or her actual injury. *Malapanis v. Shirazi*, 21 Mass. App. Ct. 378, 383–84, 487 N.E.2d 533, 537–38 (1986); *Fidler v. Eastman Kodak Co.*, 714 F.2d 192, 199 (1st Cir. 1983) (A prospective plaintiff does not need to be aware of his legal injury at this time). Rather, "[i]t is sufficient that the plaintiff has enough information *to suggest* that he has suffered an injury caused by the defendant's conduct." *Wolinetz v. Berkshire Life Ins. Co.*, 361 F.3d 44, 48 (1st Cir. 2004) (emphasis added). The relevant inquiry is whether "sufficient facts were available to provoke a reasonable person in the Plaintiff's circumstances to inquire or investigate further." *McIntyre v. United States*, 367 F.3d 38, 52 (1st Cir. 2004). The awareness of such facts must rise to something more than a mere hunch, but even something as minimal as this will establish a "duty to inquire into the possible existence of a claim in the exercise of due diligence" *Id.* (internal citations omitted). Once this duty to inquire is established, the plaintiff will be charged

"with the knowledge of what he or she would have uncovered through a reasonably diligent investigation." *Id.*

144. On May 21, 2013, Lu informed Lanza that he had learned (on May 12) that Defendants had formed their own stem cell company. ImStem filed the '551 PCT Application on June 27, 2013, and the Plaintiff had actual knowledge of this application by February 2014.

145. Further, on June 28, 2013, Kimbrel sent an email to the collaboration indicating she was aware of the Defendants formation of ImStem, as well as that she was aware that ImStem was focusing on "hESC-derived MSCs for Multiple Sclerosis."

146. Based on this evidence, it is clear that the Plaintiff and their agents knew or should have known that Wang and Xu were using the technology the Plaintiff claim as their own on June 27, 2013, and again on June 28, 2013. Indeed, as soon as the Plaintiff became aware of the Defendants forming their own stem cell company in May of 2013, it had a duty to inquire further into the Defendants' activities.

147. Furthermore, it is clear that the Plaintiff had actual knowledge of the '551 PCT Application on February 4, 2014, and therefore had actual knowledge of their harm on that date.

148. Each of these critical dates are sufficient to place the Plaintiff on notice of their injury, and each is greater than three years before the Plaintiff filed its complaint.

149. Accordingly, Plaintiff's claim in conversion is time-barred because it was filed after the three year statute of limitation proscribed by G.L. c. 260, § 2A.

150. Even if Plaintiff's conversion claim was not time-barred (it is), the Defendants did not convert the Plaintiff's property. As noted above, "[t]he elements of conversion may be established by a showing that one person exercised dominion over the personal property of

another, without right, and thereby deprived the rightful owner of its use and enjoyment." *See In re Hilson*, 448 Mass. 603, 611, 863 N.E.2d 483 (2007).

151. The Plaintiff allege that the basis for this claim is that Defendants allegedly took the Plaintiff's technology for their own use, specifically for patenting. Complaint ¶ 61 ("Defendants assumed dominion and control over Plaintiff's mesenchymal stem cell technology by claiming it as their own in the '551 patent.").

152. It is clear that the Defendants did not exercise dominion over the Plaintiff's technology without right, nor did they deprive the Plaintiff of its use. The Defendants applied for and received a patent (the '551 Patent), the narrow scope of which covers a recipe that improved upon a formula that was developed in a collaboration between the Plaintiff and Defendants (the basis of the '956 and the '321 patents). The '551 Patent does not prevent the Plaintiff from practicing or producing products that conform to the '956 or '321 Patents, which embody the Plaintiff's and Defendants' co-developed technology.

153. Moreover, "it is axiomatic that conversion is an intentional tort." *Turner v. Hubbard Sys., Inc.*, 153 F. Supp. 3d 493, 495 (D. Mass. 2015). In other words, "[i]ntent is an element of conversion that Plaintiff must allege, not a presumption that Defendant must disprove." *Id.* It is equally clear in this matter that the Defendants did not intend to deprive the Plaintiff of their property – they intended to apply for a patent application to protect their own legitimate rights and interests in the technology which is the subject of the '551 Patent. Accordingly, the Defendants did not convert the property of the Plaintiff.

2. Unjust Enrichment (Count IV)

154. As a preliminary matter, Plaintiff's unjust enrichment claim sounds in tort and is barred for the same reasons as the conversion claim. ECF 163 at 12-13. Count IV arises from the Defendants' alleged acceptance and retention of Plaintiff's "valuable intellectual property" and "asserting inventorship over Plaintiff mesenchymal stem cell technology." Am. Compl. ¶¶ 67, 68. Put simply, in Plaintiff's view, Wang and Xu took Astellas' "[HB-MSC] technology" and baked it into provisional and non-provisional patent applications, claiming it as their own. According to Plaintiff, this taking-and-patenting activity gave rise to an unjust enrichment claim.

155. Massachusetts courts have recognized that "unjust enrichment" is often a catch-all pleading and have endeavored to scrutinize such claims in order to determine whether they sound in contract or tort.[16] Many courts have ended up likening "unjust enrichment" to established equitable remedies such as (1) quantum meruit, (2) restitution, or (3) disgorgement. *See, e.g.*, *Bonina v. Sheppard*, 91 Mass. App. Ct. 622, 627, 78 N.E.3d 128, 134, *rev. denied*, 477 Mass. 1109, 89 N.E.3d 466 (2017); *Finard & Co., LLC v. Sitt Asset Mgmt.*, 79 Mass. App. Ct. 226, 230, 945 N.E.2d 404, 408 (2011).

156. This Court has previously done the same. *Cambridge Literary Properties, Ltd. v. W. Goebel Porzellanfabrik G.m.b.H. & Co. Kg.*, 448 F. Supp. 2d 244, 262 (D. Mass. 2006), *aff'd*, 510 F.3d 77 (1st Cir. 2007); *see also In re Duplication Mgmt., Inc.*, 501 B.R. 462, 488 (Bankr. D. Mass. 2013). In *Cambridge*, the Court ultimately concluded that the Plaintiff's unjust enrichment claim was **not** based in any contract relationship between the parties, but was instead based on "equitable doctrines relating [to] unjust enrichment and general principles of co-

[16] *Cf.* Restatement (Third) of Restitution and Unjust Enrichment § 1 (2011) ("It is by no means obvious, as a theoretical matter, how "unjust enrichment" should best be defined; whether it constitutes a rule of decision, a unifying theme, or something in between; or what role the principle would ideally play in our legal system. Such questions preoccupy much academic writing on the subject.")

ownership." *Id.* The Court ultimately reasoned that Plaintiff's claim was therefore more akin to a claim in "conversion or misappropriation," and therefore reasoned that the three-year statute of limitations reserved for torts should be applied to this action. *Id.*, 448 F. Supp. 2d at 263.

157. Here, the basis for the Plaintiff's claims for unjust enrichment are analogous to those addressed in *Cambridge*. The Plaintiff allege that "Defendants have been and continue to be unjustly enriched by *profiting from their wrongful conduct*. In particular, Defendants have *unlawfully used Plaintiff's property* by asserting inventorship over Plaintiff's mesenchymal stem cell technology, and deriving an unjust benefit from *exploiting Plaintiff's inventions.*" Am. Compl. ¶ 68 (emphasis added). In short, it is clear that Plaintiff base their action on alleged "wrongful," "unlawful," and exploitative use of Plaintiff's property, not on contractual grounds. *Id.* Their action, just as in *Cambridge*, is based on a theory of tortious conduct, more akin to "conversion or misappropriation." Accordingly, this Court will apply – just as the Court in *Cambridge* suggested – the statute of limitations applicable to torts, G.L. c. 260, § 2A.[17]

158. In this case, the same alleged bad acts that make up the Plaintiff's allegations in conversion are the basis of the Plaintiff's allegations in unjust enrichment. As such, the same alleged bad acts that caused the Plaintiff's claim to accrue in conversion caused the Plaintiff's claims to accrue in unjust enrichment. The Plaintiff's cause of action in unjust enrichment thus accrued on July 12, 2012, the date that the Defendants filed the first application that would become the '551 Patent.

159. Three years from the date of accrual would have been July 12, 2015. The Plaintiff did not file the instant action until November 13, 2017, over 5 years after the cause of action had accrued.

[17] This is consistent with the Court's prior Summary Judgment Order. ECF 163 at 12-13.

160. Moreover, for the same reasons set forth earlier regarding the Plaintiff's Conversion claim, the Plaintiff's claims in Unjust Enrichment would not survive the statute of limitations proscribed by G.L. c. 260, § 2A due to tolling for lack of knowledge.

161. Accordingly, Plaintiff's claim in Unjust Enrichment is past the three-year statute of limitation proscribed by G.L. c. 260, § 2A, and is therefore time barred.

162. Even if the Plaintiff's unjust enrichment claim were not time-barred (it is), the Defendants were not unjustly enriched. Plaintiff cannot prevail on its unjust enrichment claim absent the establishment, by a preponderance of the evidence, that (1) Plaintiff conferred a benefit on the Defendants; (2) Defendants appreciated or knew of the benefit; and, (3) Defendants accepted or retained the benefit under circumstances that would be inequitable. *Giles v. Ramos*, 68 Mass. App. Ct. 1105, 860 N.E.2d 978 (2007).

163. Plaintiff also has the burden of demonstrating via a preponderance of the evidence that Defendants were "unjustly enriched by the acquisition of title to identifiable property at the expense of [Plaintiff] or in violation of the [Plaintiff's] rights." Restatement (Third) of Restitution and Unjust Enrichment § 55(1), at 296 (2011). In other words, Plaintiff cannot prevail on this claim without proving the amount of Defendants' benefit or gain. *See, e.g.*, *Bonina v. Sheppard*, 78 N.E.3d 128, 134 (Mass. App. Ct. 2017); *see also Invest Almaz v. Temple-Inland Forest Prods. Corp.*, 243 F.3d 57, 70 (1st Cir. 2001).

164. Neither party has commercialized or received any revenue from HB-MSCs in general. Plaintiff has not commercialized or otherwise received any revenue from the inventions claimed in the '321 or '956 patents. Similarly, ImStem has not commercialized or obtained any revenue from the inventions claimed in the '551 patent. There is no profit that could be disgorged.

165. As neither party has commercialized or otherwise earned revenue related to the HB-MSCs, Plaintiff's expert based his opinion of damages on the "implied value" of ImStem and further assumes that this entire "implied value" of ImStem is attributable to the value of property that Plaintiff purportedly conferred on Defendants.

166. The value of ImStem is not, however, based upon HB-MSCs generally or the patents at issue in this case, specifically.

167. The value of ImStem arises out of Dr. Xu's reputation and ImStem's work with T-MSCs. As such, even if one assumed, *arguendo*, that a benefit was conferred upon the Defendants, the evidence does not support that the Defendants accepted or retained that benefit under inequitable circumstances. Instead, the value of ImStem is in whole or in part, founded upon Dr. Xu's own reputation and on Defendants' own property in its work with T-MSCs.

168. Plaintiff's expert's assumption that ImStem's value is based solely on Plaintiff's property renders it insufficient to establish damages for unjust enrichment because it fails to apportion any value for Dr. Xu's reputation and/or the value of ImStem's work with T-MSCs.

169. Absent apportionment for Dr. Xu's reputation and the value of T-MSCs with a reasonable degree of certainty, the Court cannot establish damages without improperly speculating on the value thereof. As the Plaintiff has failed to meet their burden, the Court finds for Defendants on this Count. *See Invest Almaz*, 243 F.3d at 70 (inadequate evidence of value obtained by a defendant precludes a finding in favor of the plaintiff for a restitution claim).

3. Unfair Trade Practices Under c. 93A (Count V)

170. Plaintiff also assert one count of Unfair Trade Practices under M.G.L. c. 93A (Count V).[18] As with the other state law claims, the statute of limitations prevents Plaintiff from prevailing on this claim. Plaintiff's claim arising under Mass. G.L. 93A is subject to a four-year statute of limitations. M.G. L. c. 260, § 5A. ECF 163 at 12-13. The accrual date for a Chapter 93A claim is determined by the same principles as for a tort action. *See Int'l Mobiles v. Carroon & Black/Fairfield*, 29 Mass.App.Ct. 215, 221, 560 N.E.2d 122 (1990) ("the loss which the plaintiff must show in a c. 93A action is analogous, if not identical, to the appreciable harm the plaintiff sustains in a negligence action . . . . when the plaintiff knew or should have known of appreciable harm resulting from the defendant's [actions]."). The relevant event "starting the clock" is the moment a Plaintiff suffers a loss connected to an unfair or deceptive act. *See International Fid. Ins. Co. v. Wilson*, 387 Mass. 841, 850, 443 N.E.2d 1308 (1983). Indeed, it has long been established that "[t]he law ministers to the vigilant not to those who sleep upon perceptible rights." *Puleio v. Vose*, 830 F.2d 1197, 1203 (1st Cir. 1987).

171. In support of this claim, the Plaintiff alleges that:

> Defendants have engaged in unfair acts and practices pursuant to Massachusetts General Laws. c. 93A, which include, without limitation, unjust enrichment and conversion, as set forth in this Complaint. For example, Defendants have improperly used Plaintiffs' proprietary information in filing of patent applications whereby they took Plaintiffs' innovations and technologies relating to mesenchymal stem cells for themselves.

Am. Compl. ¶ 73; *cf. id. at* ¶¶ 50 and 80 (asserting the same allegation of taking Plaintiff's intellectual property and passing it as their own by filing patent applications).

[18] The claim is essentially a restatement of Astellas' earlier state-law claims. It adds little. Even the alleged harm suffered is the same. *See Am. Compl.* ¶ 75 ("loss of value of the rights to any patents based on Plaintiffs' mesenchymal stem cell intellectual property and proprietary information").

172. Based on the evidence presented and the pleadings, the same alleged bad acts that make up the Plaintiff's allegations in conversion and unjust enrichment are the basis of the deceptive and unfair acts or practices that sustain the Plaintiff's allegations under Mass. G.L. 93A. As such, the same alleged bad acts that caused the Plaintiff's claim to accrue in Conversion and Unjust Enrichment caused the Plaintiff's claims to accrue under Mass. G.L. 93A. Therefore, the Plaintiff's cause of action under Mass. G.L. 93A accrued on July 12, 2012, the date that the Defendants filed the first application that would become the '551 Patent.

173. Four years from the date of accrual would have been July 12, 2016. The Plaintiff did not file the instant action until November 13, 2017, over five years after the cause of action had accrued.

174. Thus, for the same reasons set forth in earlier in this opinion regarding the Plaintiff's Conversion and Unjust Enrichment claims, this Court further finds that the Plaintiff's claim under Mass. G.L. 93A would not survive the statute of limitations proscribed by M.G. L. c. 260, § 5A due to tolling for lack of knowledge.

175. As with the tort claims, Astellas cannot credibly toll the statute of limitations through an alleged lack of knowledge. Plaintiff needed only to be aware of facts which would suggest that he/she has been injured. *Bowen*, 557 N.E.2d at 741; *Szymanski*, 56 Mass. App. Ct. at 371 (2002); *Stark*, 736 N.E.2d at 442. First, on May 21, 2013, Plaintiff learned that the Defendants had created their own stem cell company. This was sufficient to alert Plaintiff that Defendants were using their stem cell "innovations and technologies" in an unfair or deceptive manner. Then, on June 27, 2013, Wang and Xu filed the '551 PCT Application. The next day, Kimbrel emailed Vincent telling him to "keep an eye" on the "UConn patent pending", in which Kimbrel mentioned ImStem by name, and noted that she was aware of ImStem's purpose to

"continue exploring hESC-derived MSCs." Plaintiff therefore had sufficient information at this time to know that Defendants were (allegedly) using their stem cell "innovations and technologies" in an unfair manner. Plaintiff could, at the very least, have investigated further. They did not.

176. Plaintiff had numerous opportunities to seek redress for their injury in a time frame that was not barred by Massachusetts law. They failed to do so at every turn. "The law ministers to the vigilant not to those who sleep upon perceptible rights." *Puleio v. Vose*, 830 F.2d 1197, 1203 (1st Cir. 1987).

177. Accordingly, Plaintiff's claim under Mass. G.L. 93A is past the four year statute of limitation proscribed by M.G. L. c. 260, § 5A, and is therefore time barred.

178. Even if the Plaintiff's unfair trade practice claim were not time-barred (it is), Defendants cannot be liable for a violation of that chapter. To bring a claim under Chapter 93A, a plaintiff must show (1) a deceptive or unfair "act or practice on the part of the defendant," (2) "an injury or loss suffered by the consumer," and (3) causation. *Marti v. Schreiber/Cohen, LLC*, No. 4:18-40164-TSH, 2020 WL 1877954, at *3 (D. Mass. Apr. 15, 2020). Additionally, it is required that the "the unfair and deceptive practices occurred primarily and substantially in Massachusetts." *Kuwaiti Danish Computer Co. v. Digital Equip. Corp.*, 438 Mass. 459, 471 (2003); *Shea v. Millett*, No. 17-CV-12233-ADB, 2018 WL 2077599, at *4 (D. Mass. May 3, 2018) ("In the absence of at least some assertion that the conduct giving rise to the Chapter 93A violation occurred in, was intended to influence behavior in, or was designed to cause losses in Massachusetts, the allegations are not sufficient to state a Chapter 93A claim.").

179. The Plaintiff alleges that this claim arises from the same conduct (*i.e.*, allegedly taking the Plaintiff's technology) that makes up the basis of their conversion and unjust enrichment counts.

180. The Defendants were not engaged in a deceptive or unfair trade practice. They did not employ deception, or an unfair act or practice, in patenting the technology that makes up the '551 patent, as they have a proper ownership interest in this technology.

181. Moreover, it is clear that no injury or loss was suffered by the Plaintiff. The '551 Patent does not prevent Astellas from using or marketing their technology, which is embodied in the '956 and '321 patents, nor has the PTO's grant of the '551 Patent negatively affected Massachusetts consumers in any meaningful way.

182. As no injury was suffered or sustained, the element of causation is moot.

183. Even if there were an alleged injury, the acts or practices that make up the foundation of the Plaintiff's claims did not occur primarily and substantially in Massachusetts. Only Astellas maintains a location in Massachusetts, though it is headquartered in Northbrook, Illinois, and is merely the U.S. affiliate of a global pharmaceutical company based in Tokyo, Japan. Defendants Xu and Wang were located outside the Commonwealth of Massachusetts during the filing of the '551 patent (and at all relevant times during this case). Defendant ImStem is a corporation organized under the laws of the State of Connecticut, with a principal place of business in Farmington, Connecticut, and no offices in Massachusetts. Wang lives and works in Connecticut, and Xu previously lived and worked in Connecticut (now in Macau). The filing of the '551 Patent and all predecessor applications were done to the USPTO, which is not headquartered in Massachusetts. The weight of the evidence does not illustrate that the conduct

during or leading up to the filing of the '551 or its predecessor applications "occurred in, was intended to influence behavior in, or was designed to cause losses in Massachusetts."

184. To the extent the Plaintiff claims that acts or practices by the Defendants during the collaboration period rise to the level of a violation of Mass. G.L. 93A, this conduct was still situated primarily outside of the Commonwealth of Massachusetts. Defendants' contribution to the '956 patent and the '321 patent – which the Plaintiff claims was limited to the administration of the EAE model – were conducted primarily at Dr. Xu's laboratory at the University of Connecticut, which is not in Massachusetts. The weight of the evidence indicates no design or intent on the part of the Defendants to influence or cause harm in the State of Massachusetts.

185. Accordingly, the Defendants did not violate Mass. G.L. 93A.

4. All of Plaintiff's State Law Claims are Preempted by Federal Patent Law (Counts III-V)

186. All three of Plaintiff's state law claims suffer another fatal flaw: They are all preempted by federal patent law. The Federal Circuit has explained that "although federal patent law plainly does not provide for explicit preemption [...] a state may not offer patent-like protection to intellectual creations that would otherwise remain unprotected as a matter of federal law." *Univ. of Colorado Found., Inc. v. Am. Cyanamid Co.*, 196 F.3d 1366, 1035 (Fed. Cir. 1999); *id.* at 1371 (whether a state law claim is preempted by federal patent law is governed by the law of the Federal Circuit).

187. Critically, the Federal Circuit has held that "the field of federal patent law preempts any state law that purports to define rights based on inventorship." *HIF Bio, Inc. v. Yung Shin Pharm. Indus. Co.*, 600 F.3d 1347, 1353 (Fed. Cir. 2010). Inventorship disputes pose uniquely difficult issues for the purposes of a preemption analysis. *Mass. Eye & Ear Infirmary v. QLT Phototherapeutics, Inc.*, 412 F.3d 215, 235 (1st Cir. 2005) ("We recognize that the

preemption issue here is close."). In *Mass. Eye & Ear Infirmary*, the Court determined that the presence of an agreement between the parties which governed their respective obligations in future patenting activities may save a state law claim from preemption. *Id.*; *see Ultra-Precision Mfg., Ltd. v. Ford Motor Co*., 411 F.3d 1369, 1379 (Fed. Cir. 2005)). Here, however, there was no such agreement; indeed, Plaintiff has expressly dropped their breach of contract claim.

188. Other courts have precluded state-law claims tacked onto inventorship disputes. In the case of state law claim in conversion, the claim is preempted if the "claim is both 'patent-like' in nature, and also turns on a determination of inventorship regarding the . . . design at issue." *Speedfit LLC v. Woodway USA, Inc.*, 226 F. Supp. 3d 149, 160 (E.D.N.Y. 2016). In *Speedfit*, the court found that a state-law conversion claim premised on the idea that the Defendant "has wrongfully exercised dominion over the property of Plaintiff by refusing to name Astilean and Bostan as either inventors or joint inventors" was preempted by Federal patent law, as the "plaintiffs' assertion of ownership [and thus conversion] . . . clearly turns on a determination of inventorship." *Id.*; *cf. Lyden v. Nike Inc*., 2014 WL 2563401, *3 (D. Or. 2014), *denying reconsideration*, 2014 WL 4631206 (D. Or. Sep. 15, 2014) (finding that where "Plaintiff allege[d] that Defendant . . . converted his intellectual property by securing patents from the PTO for the same subject matter as Plaintiff's patents and patent applications that he had shared with . . . [Defendant] in 2002" was preempted.). Here too, the matter of Plaintiff's conversion claim is dependent on this Court determining inventorship.

189. A state law claim in unjust enrichment is similarly preempted if the claim requires that this Court first resolve a question of inventorship before it can resolve the unjust enrichment claim. To that end, the court in *OptoLum, Inc. v. Cree, Inc.* found that "[b]ecause OptoLum's unjust enrichment claim depends on the determination that OptoLum, not Cree, invented the

LED technology at issue here, the claim is preempted by federal patent law." 244 F. Supp. 3d 1005, 1014 (D. Ariz. 2017) (collecting cases). Here too, the matter of Plaintiff's unjust enrichment claim is dependent on this Court determining inventorship.

190. Finally, with regard to Mass. G.L. 93A, it is clear that the Plaintiff intends the same alleged misconduct pleaded in their Conversion and Unjust Enrichment counts to make up the body of their claim under Mass. G.L. 93A. Am. Compl. ¶ 73. The Court finds nothing unique about a state law regulating unfair competition which would change this Court's approach. *See Sorias v. Nat'l Cellular USA, Inc*., 124 F. Supp. 3d 244, 262 (E.D.N.Y. 2015) (finding a state unfair competition claim preempted as it "Plaintiff's make no allegations of unfair competition that are 'separate and independent from its patent law claim' of infringement"). As such, this claim too is dependent on this Court determining inventorship.

191. Accordingly, the Plaintiff's state law claims, based in Conversion (Count III), Unjust Enrichment (Count IV), and Unfair Trade Practices under Mass. G.L. 93A (Count V), are preempted, as each define a right based upon who invented the technology at issue.

5. All of Plaintiff's State Law Claims are Barred by the Affirmative Defenses of Laches and Unclean Hands

192. All three of Plaintiff's state law claims suffer another fatal flaw: They are barred by the doctrine of laches. The Plaintiff's delay in filing a lawsuit was unjustified, unreasonable and has prejudiced the Defendants. *See Melrose Fish & Game Club, Inc. v. Tennessee Gas Pipeline Co*., LLC, 89 Mass. App. Ct. 594, 602, 52 N.E.3d 1089, 1096 (2016).

193. As noted above, Plaintiff knew about its potential claims for years, describing it as an "airtight" case. Nevertheless, the Plaintiff not only made the strategic decision not to file a lawsuit, it also chose not to notify the Defendants of its concerns. It made no inquiry about the

nature of the Defendants' operations, let alone requesting that the Defendants not make—what it now claims—unauthorized use of the technology.

194. Meanwhile, the Defendants continued with their business plans and their attempts to commercialize its TSMC technology. If Plaintiff had provided notice to the Defendants of its concerns, the Defendants would have been able to address those concerns in real time. Plaintiff is trying to affirmatively capitalize on its failure to provide timely notice to the Defendants of their purported wrongdoing.

195. The Plaintiff's claims for equitable relief are barred by the doctrine of unclean hands. The Plaintiff's bad faith bars the recovery it seeks. *See Fid. Mgmt. & Research Co. v. Ostrander*, 40 Mass. App. Ct. 195, 200, 662 N.E.2d 699, 704 (1996).

6. Plaintiff's Damages Assertions Are Unavailing

196. All three of Plaintiff's state law claims suffer another fatal flaw: Plaintiff has not suffered any cognizable harm. It is worth repeating the basic fact above that no one has commercialized the disputed technology, no one has alleged a lost sale, lost a license, lost a customer, etc. Both parties contributed time and money to the venture, and both benefited from it. Aside from a few bruised egos, no one has been harmed.

197. Moreover, under Massachusetts law a "plaintiff has the burden of damages 'with reasonable certainty.'" *Coady v. Wellfleet Marine Corp.*, 62 Mass.App.Ct. 237, 245, 816 N.E.2d 124 (2004) (quoting *Agoos Leather Cos. v. American & Foreign Ins. Co.*, 342 Mass. 603, 608, 174 N.E.2d 652 (1961)). Although "proof of damages does not require mathematical precision, it must be based on more than mere speculation." *Squeri v. McCarrick*, 32 Mass.App.Ct. 203, 209, 588 N.E.2d 22 (1992). In other words, a Plaintiff is "entitled to compensation for all damages that reasonably are to be expected to follow, but not to those that possibly may follow." *Reckis v. Johnson & Johnson*, 471 Mass. 272, 299, 28 N.E.3d 445, 467 (2015).

198. Plaintiff's entire damages theory is based on it seeking to recover the "paper value" of ImStem. They only way Plaintiff's argument works is if 100% of the investment in InStem was because of Defendants' use of Plaintiff's alleged intellectual property prior to publication of the Lanza/Kimbrel patent application on June 6, 2013 (and was therefore disclosed publicly). If there is value in ImStem that is separate and apart from Defendants' alleged bad acts, some of the value of Imstem must be apportioned to those other areas to get a true measure of damages. Based on the evidence reviewed, including the other information in the record about the reasons ImStem's investors actually invested (Xu's reputation, T-MSCs, etc), the Court concludes that the value of ImStem as of June 6, 2013 was not completely based on Defendants' alleged misdeeds. Because of this, and because there is nothing to tie each of the causes of action to actual damages (Plaintiff assumes, without any real analysis, that all damages for the state law claims are identical), Plaintiff has failed to do any apportionment, the Court concludes that Plaintiff's damages claim is too speculative to allow recovery.

199. Accordingly, the Court finds that the Plaintiff's damages premised upon the Defendants alleged diversion of possible investments and/or investors are speculative.

V. Defendants' Unjust Enrichment Counterclaim

200. Defendants also bring a counterclaim in Unjust Enrichment (ECF 91). As discussed above, a claim seated in Unjust Enrichment can take many forms. *See* Restatement (Third) of Restitution and Unjust Enrichment § 1 (2011) ("It is by no means obvious, as a theoretical matter, how "unjust enrichment" should best be defined; whether it constitutes a rule of decision, a unifying theme, or something in between; or what role the principle would ideally play in our legal system. Such questions preoccupy much academic writing on the subject."). One – such as the one brought by the Plaintiff – is tortious in nature. However, another is recognized as equitable. *See O'Hara v. Diageo-Guinness, USA, Inc.*, 306 F. Supp. 3d 441, 466

(D. Mass. 2018); *see Mass. Eye & Ear Infirmary v. QLT Phototherapeutics, Inc.*, 552 F.3d 47, 57 (1st Cir. 2009) ("Massachusetts courts emphasize the primacy of equitable concerns in a finding of unjust enrichment . . . ."). The remedy for this flavor of unjust enrichment is restitution. *Santagate v. Tower*, 64 Mass. App. Ct. 324, 336, 833 N.E.2d 171, 180 (2005). *See also* Restatement (Third) of Restitution and Unjust Enrichment § 4 (2011).

201. But "restitution is not damages." *Santagate*. It is "a restoration required to prevent unjust enrichment." *Id.* "The fundamental substantive basis for restitution is that the defendant has been unjustly enriched by receiving something, tangible or intangible, that properly belongs to the plaintiff." *Id.* Accordingly, "[r]estitution rectifies unjust enrichment by forcing restoration to the plaintiff." *Id.*

202. In this matter, there has been an unjust enrichment. The Plaintiff has received the benefit of the Defendants' knowledge and expertise in the days leading up to the prosecution of the 321 and '956 patents. They have not given the Defendants proper credit, payment, or ownership rights in exchange.

203. The Plaintiff has the burden of proving each of the elements of its claim against the Defendants by clear and convincing evidence.

204. For the reasons articulated above with respect to its other state law claims, Plaintiff has to carry its burden of proof with respect to its claims against the Defendants. In fact, Plaintiff's claim that it is entitled to the "paper value" of ImStem years after the collaboration ended (and up to today) is even further afield, as the evidence demonstrates that the role and value of Defendants' T-MSC technology (and patents) is the real value of the company.

205. Judgment is entered on behalf of the Defendants with respect to each of the Plaintiff's claims.

206. The Defendants had the burden of proving each of the elements of their counterclaims against the Plaintiff by clear and convincing evidence.

207. The Defendants have carried their burden of proof with respect to the claims in their Counterclaim. Drs. Xu and Wang should be added to the '321 patent and Dr. Wang should be added to the '956 patent.

CONCLUSION

WHEREFORE, for the reasons set forth above, the Defendants respectfully request that the Court accept the Defendants' proposed Findings of Fact and Conclusions of Law and incorporate them into a decision entering judgment in favor of the Defendants. Specifically, the Defendants ask that Drs. Xu and Wang remain on the '551 patent, that they be added to the '321 patent, Dr. Wang be added to the '956 patent, and that the Plaintiff's state law clams be dismissed with prejudice.

Dated: August 10, 2020

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CERTIFICATE OF SERVICE

I hereby certify that on August 10, 2020, I caused a true copy of the foregoing document to be served upon all counsel of record via the Court's CM/ECF electronic filing system.

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